Risk Factors for Rebleeding in Peptic Ulcer Bleeding: A Second Look at Second-Look Endoscopy

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Rebleeding, which occurs in 10–15 % of patients with peptic ulcer bleeding (PUB) [1], is associated with a two- to fivefold mortality increase, depending on the presence of other risk factors [2]. Therefore, identification of the predictors of rebleeding seems meaningful in order to identify high-risk patients needing close observation and rapid treatment in case of the development of rebleeding.

According to previous studies, hemodynamic shock, usually defined as a systolic blood pressure <100 mmHg, often combined with tachycardia >100 beats/min, is the most powerful pre-endoscopic predictor of rebleeding [3, 4]. In a meta-analysis, hemodynamic shock was associated with an odds ratio (OR) of rebleeding of 3.3 [3]. Conversely, studies on the association between anemia and rebleeding have found conflicting results: Some of the existing data indicate that hemoglobin <10 g/L may be associated with an increased risk of rebleeding [3]. Data concerning the risks of transfusion are even more confounded by differing study protocols (e.g., pre- or post-endoscopic transfusion, different categorization of volume) to the point that the rebleeding risk of pre-endoscopic transfusion is unknown. Regarding endoscopic predictors, active bleeding at endoscopy (OR 1.7), ulcer size >2 cm (OR 2.8), posterior duodenal ulcer location (OR 3.8), and high lesser gastric curvature ulcer location (OR 2.9) all predict rebleeding in a meta-analysis [3].

The type of endoscopic treatment applied does also affect the risk of rebleeding. A Cochrane analysis reported that combination of epinephrine injection with a second

endoscopic treatment modality reduces the relative risk (RR) of rebleeding or persistent bleeding (RR 0.57) compared to endoscopic treatment with epinephrine alone [5]. Therefore, endoscopic monotherapy with injection of epinephrine should be avoided.

In a meta-analysis based on eight randomized controlled trials (RCTs) published from 1994 to 2006, performance of second-look endoscopy within 16–48 h was associated with a significant reduction in rebleeding rate (OR 0.55) [6]. Generalization of this finding to current practice standards can be questioned because only one of the included studies used endoscopic combination therapy combined with high-dose infusion of proton-pump inhibitors [7]. Furthermore, detailed review of the fully published component studies revealed that a significant reduction in rebleeding was only evident in two studies that included patients with a very high risk of rebleeding (up to 47 % of included patients had hemodynamic shock) [6]. When these two trials were excluded from the meta-analysis, the association between performance of second-look endoscopy and rebleeding became statistically insignificant [6]. In a cost-effectiveness analysis, performance of second-look endoscopy was only cost-effective after therapeutic endoscopy if the risk of rebleeding was greater than 31 % [8].

In this issue of *Digestive Diseases and Sciences*, Kim et al. [9] published a prospective multicenter study of risk factors for rebleeding among 699 patients with PUB from Forrest classification [10] Ia–IIb ulcers. Using multivariate logistic regression analysis, the authors reported that performance of second-look endoscopy was associated with a lower risk (OR 0.269) of rebleeding. High transfusion volume (above 5 units) and use of nonsteroidal anti-inflammatory drugs (NSAIDs) were both associated with a fourfold increase in risk of rebleeding. The authors

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concluded that performance of second-look endoscopy seemed to lower the risk of rebleeding in high-risk PUB. Therefore, the authors suggest that routine second-look endoscopy should be considered and more concern should be paid to patients receiving >5 units of transfusion and taking NSAIDs.

The finding that NSAIDs and transfusion may increase the risk of rebleeding confirms previous studies [11, 12], reinforcing the likelihood that these patients are at an increased risk of poor outcome. The validity of the authors' conclusion on the routine use of second-look endoscopy can be questioned because of limitations in design (non-RCT) and methods, including no clear definition of rebleeding, differences in indications used for performing second-look endoscopy between centers, and incomplete adjustment for confounding factors of relevance.

Should endoscopists perform routine second-look endoscopy in all patients with Forrest I–IIb ulcers? Based on the current literature, I believe the answer is “no.” There is evidence supporting that performance of second-look endoscopy in patients with a very high risk of rebleeding is associated with a reduced rate of rebleeding, a reduced need for surgery, and saving of net costs [6, 8]. In my view, second-look endoscopy can be considered in selected patients with high risk of rebleeding, in particular if the primary endoscopic treatment was suboptimal (e.g., monotherapy with epinephrine, compromised lesion visualization). Well-powered RCTs demonstrating a clinically significant effect of second-look endoscopy in an updated setting are needed before routine use of this procedure in all patients with Forrest I–IIb lesions can be recommended.

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